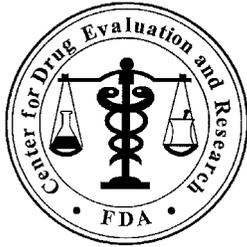


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-037

PROPRIETARY NAME REVIEW(S)



Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date: August 26, 2009

To: Thomas Laughren, MD, Director
Division of Psychiatry Products

Through: Carlos Mena-Grillasca, RPh, Acting Team Leader
Denise P. Toyer, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Walter Fava, R.Ph., Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Intuniv (Guanfacine Hydrochloride) Extended-release Tablet
1 mg, 2 mg, 3 mg, 4 mg

Application Type/Number: NDA 22-037

Applicant: Shire Pharmaceuticals

OSE RCM #: 2009-1367

CONTENTS

1	INTRODUCTION.....	3
2	METHODS AND RESULTS.....	3
3	CONCLUSIONS AND RECOMMENDATIONS.....	3
4	REFERENCES.....	4

1 INTRODUCTION

This review is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Intuniv, acceptable in OSE Review #2009-256, dated May 5, 2009. Since that review, none of Intuniv's product characteristics have been altered. Additionally, on August 6, 2009, DDMAC reviewed the proposed name and had no concerns regarding the proposed name from a promotional perspective and did not offer any additional comments relating to the proposed name. Furthermore, the review Division did not have any concerns with the proposed name, Intuniv during our initial review.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. Additionally, DMEPA searches the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors. We used the same search criteria used in OSE Review #2009-256 for the proposed proprietary name, Intuniv.

The searches of the databases did not yield any new names thought to look or sound similar to Intuniv and represent a potential source of drug name confusion.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of August 17, 2009.

3 CONCLUSIONS AND RECOMMENDATIONS

The re-review of Intuniv did not identify any additional names thought to look or sound similar to the proposed name since our last review. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Intuniv, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Psychiatry Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4 REFERENCES

1. OSE review # 2009-256 Proprietary Name Review of Intuniv; Walter Fava, Safety Evaluator.

2. **Drugs@FDA** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present.

Drugs@FDA contains official information about FDA approved [brand name](#), [generic drugs](#), [therapeutic biological products](#), [prescription](#) and [over-the-counter](#) human drugs and [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

3. **Electronic online version of the FDA Orange Book** (<http://www.fda.gov/cder/ob/default.htm>)

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

4. **USAN Stems** (<http://www.ama-assn.org/ama/pub/category/4782.html>)

USAN Stems List contains all the recognized USAN stems.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

WALTER L FAVA
08/26/2009

CARLOS M MENA-GRILLASCA
08/26/2009

DENISE P TOYER
08/26/2009



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

Date: May 5, 2009

To: Thomas Laughren, Director
Division of Psychiatry Products

Through: Carlos Mena-Grillasca, R.Ph., Acting Team Leader
Denise Toyer, Pharm.D., Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Walter Fava, R.Ph., Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Intuniv (Guanfacine Hydrochloride) Extended-release Tablets
1 mg, 2 mg, 3 mg, 4 mg

Application Type/Number: NDA #: 22-037

Applicant/Applicant: Shire Pharmaceuticals

OSE RCM #: 2009-256

***** This document contains proprietary and confidential information that should not be released to the public.*****

CONTENTS

EXECUTIVE SUMMARY	2
1 BACKGROUND	2
1.1 Introduction	2
1.2 Product Information	2
2 METHODS AND MATERIALS	2
2.1 Proprietary Name Risk Assessment	3
3 RESULTS	8
3.1 Proprietary Name Risk Assessment	8
4 DISCUSSION	8
4.1 Proprietary Name Risk Assessment	9
5 CONCLUSIONS AND RECOMMENDATIONS	9
5.1 Comments To the Division	9
5.2 Comments To The Applicant	10
6 REFERENCES	11
APPENDICES	12

EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment for this pre-action proprietary name review found that the proposed name, Intuniv, is not vulnerable to name confusion that could lead to medication errors. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Intuniv, for this product.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and recommends that the name be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change.

In addition, the proposed name must be reevaluated 90 days before approval of the NDA, even if the proposed product characteristics as stated in this review are not altered.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Psychiatry Products for an assessment of the proposed proprietary name, Intuniv, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. The Applicant also submitted container labels, carton and package insert labeling for review. The labels and labeling will be reviewed under separate cover in forthcoming review OSE Review #2009-257.

1.2 REGULATORY HISTORY

DMEPA previously reviewed the proposed proprietary name, Intuniv, in OSE Review # 2006-821 dated April 18, 2007, and found the name acceptable. (b) (4)

1.3 PRODUCT INFORMATION

Intuniv (guanfacine hydrochloride) is a selective alpha-2A-adrenergic receptor agonist indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). It is available in extended-release tablets and is dosed once a day. The recommended starting dose is 1 mg per day and dose adjustments of no more than 1 mg per week are recommended. The usual maintenance dose is between 1 mg and 4 mg per day. Intuniv will be available in 1 mg, 2 mg, 3 mg and 4 mg tablets. Tapering in decrements of no more than 1 mg every 3 days to 7 days is recommended if the drug needs to be discontinued.

2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment (See 2.1 Proprietary Name Risk Assessment). The primary objective for the assessment is to identify and remedy potential sources of medication error prior to drug approval. DMEPA defines a medication error as any preventable event

that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center.

For the proposed proprietary name, DMEPA staff searched a standard set of databases and information sources to identify names with orthographic and phonetic similarity (See 2.1.1 for details) and held a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). DMEPA staff also conducts internal FDA prescription analysis studies. When provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (See 2.1.3 for details). The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.² FMEA is used to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment since the product characteristics may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to, established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

¹ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

² Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

³ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

2.1.1 Search Criteria

The DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter ‘I’ when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.^{4,5}

To identify drug names that may look similar to Intuniv, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (7 letters), and upstrokes (2 letters; the capital letter ‘I’ and the lower case letter ‘t’). Additionally, several letters in Intuniv may be vulnerable to ambiguity when scripted, including the capital letter ‘I’ may appear as upper case letters ‘S’, ‘O’, ‘J’, ‘A’, ‘T’, or ‘P’, and as the lower case letters ‘l’ or ‘e’; lower case ‘n’ may look like lower case ‘m’, ‘v’, ‘r’ or ‘u’; lower case ‘t’ may look like lower case ‘l’, ‘x’, or ‘r’; lower case letter ‘u’, may look like lower case letters ‘a’, ‘n’, ‘v’, or ‘w’; lower case letter ‘i’ may appear as lower case ‘e’, and the lower case letter ‘v’ may appear as the lower case letters ‘u’, ‘n’, ‘w’, ‘y’ or ‘r’. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Intuniv.

When searching to identify potential names that may sound similar to Intuniv, the DMEPA staff search for names with similar number of syllables (three), stresses (IN-tun-IV or in-TUN-iv or in-tun-IV), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as the letter ‘I’ may sound like the letters ‘U’, ‘E’ or ‘O’, and the letter ‘n’ may sound like the letter ‘m’ and the letter ‘t’ may sound like the letter ‘d’, the letter ‘u’ may sound like the letter ‘o’ and the letter ‘v’ may sound like the letters ‘f’ or ‘ph’. The Applicant’s intended pronunciation of the proprietary name was not provided with the proposed name submission and, therefore, could not be taken into consideration. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

The DMEPA staff also considers the product characteristics associated with the proposed drug throughout the identification of similar drug names because the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the following information was provided about the proposed product to the medication error staff: proposed proprietary name (Intuniv), proposed established name (guanfacine hydrochloride), proposed indication of use (Attention Deficit Hyperactivity Disorder), strength (1 mg, 2 mg, 3 mg and 4 mg), dose (1 mg to 4 mg), frequency of administration (once a day), route (oral), and dosage form (extended-release tablet). Appendix A provides a more detailed listing of the product characteristics the medication error staff generally takes into consideration.

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, these broader safety implications of the name are considered and evaluated throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

⁴ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁵ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

2.1.1.1 Database and Information Sources

The proposed proprietary name was provided to the DMEPA staff to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1.1. A standard description of the databases used in the searches is provided in Section 6. To complement the process, the medication error staff used a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff reviewed the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators were then pooled and presented to the CDER Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention and Analysis (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed.

The pooled results of the DMEPA staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.1.2 Comments from the OND review Division or Generic drugs

DMEPA requests the regulatory division in the Office of New Drugs responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. Any comments or concerns are addressed in the safety evaluator's assessment.

The regulatory division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The regulatory division is requested to concur/not concur with DMEPA's final decision.

2.1.3 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1, the Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Mode and Effects Analysis and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name as a result of the name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug

⁶ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking:

“Is the name Intuniv convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?”

An affirmative answer indicates a failure mode and represents a potential for Intuniv to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the name possesses similarity that would cause confusion at any point in the medication use system, then the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking:

“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”

The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies; for example, product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

DMEPA will object to the use of proposed proprietary name when one or more of the following conditions are identified in the Safety Evaluator’s Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise. [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
2. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

4. The proposed proprietary name contains an USAN (United States Adopted Names) stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product is awarded approval first has the right to the use of the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these criteria are met, then DMEPA will not object to the use of the proprietary name. If any of these criteria are met, then DMEPA will object to the use of the proposed proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP), who have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval.

Furthermore, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational and other post-approval efforts are low-leverage strategies that have proven to have limited effectiveness at alleviating medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Applicants have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. (See Section 4 for limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The searches yielded a total of 22 names as having some similarity to the name Intuniv.

Twenty of the names were thought to look like Intuniv. These include (b) (4) Intron A, Introcin, Interac, Entumin, Infarix, Interex, Entereg, Invanz, Intropin, Intelence, Antara, Intal, Emtriva, Indocin, Entecavir, Intrinsa, Insulin, Infuvite, and Indinavir. The remaining two names, Entuniv and Imatinib were thought to look and sound similar to Intuniv.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of February 19, 2009.

3.1.2 CDER Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Intuniv.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.1.3 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator resulted in no additional names which were thought to look or sound similar to Intuniv and represent a potential source of drug name confusion. However, since the Applicant will not market the 2.5 mg and 3.5 mg tablets, DMEPA re-reviewed the fifteen names previously identified in OSE review # 2006-821. Ten of the fifteen names previously identified were also identified by EPD panel members for the current review. The five remaining names, Actinex, Lotrisone, Imodium, Lotrimin, and Enjuvia, were previously identified as having look-alike similarity with Intuniv. Thus, 27 names were analyzed to determine if the drug names could be confused with Intuniv and if the drug name confusion would likely result in a medication error.

Additionally, the primary Safety Evaluator considered the risk to patients currently taking guanfacine immediate-release tablets who may be switched to Intuniv (guanfacine extended-release) tablets by their prescriber.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

Twenty seven names were evaluated for their potential similarity to the proposed name, Intuniv. Four names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix B). Failure mode and effect analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with any of the remaining 23 names and lead to medication errors. This analysis determined that the name similarity between Intuniv was unlikely to result in medication errors with any of the 23 products identified for the reasons presented in Appendices C through G.

DMEPA also considered the risk to patients currently taking guanfacine immediate-release tablets who may be switched to Intuniv (guanfacine extended-release) tablets by their prescriber. Upon launch of this new formulation, Intuniv may be perceived as being more beneficial than the guanfacine immediate-release tablets. However, both products are dosed at a once a day frequency; the relative bioavailability of Intuniv to immediate release guanfacine is 58%, and generic equivalents are available for immediate release guanfacine. Thus patients taking immediate release guanfacine for hypertension are less likely to be switched to Intuniv because there are no benefits. Although, the draft insert labeling initially contained directions for switching patients from the immediate release formulation to the extended release formulation DMEPA has learned from DPP that these directions have been removed from the insert labeling. Thus, our concerns on switching patients from the immediate release formulation to the extended release formulation are minimized.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed proprietary name, Intuniv, is not vulnerable to name confusion that could lead to medication errors. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Intuniv, for this product at this time. Additionally, DDMAC does not object to the proposed name, Intuniv, from a promotional perspective.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. If the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

5.1 COMMENTS TO THE DIVISION

We are willing to meet with the Division for further discussion, if needed. Please copy DMEPA on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Abolade Adeolu, Project Manager, at 301-796-4264.

5.2 COMMENTS TO THE APPLICANT

5.2.1 *Proprietary Name*

We have completed our review of the proposed proprietary name, Intuniv, and have concluded that it is acceptable. DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, Intuniv will be re-reviewed prior to the approval date. If we find the name unacceptable following the re-review, we will notify you.

6 REFERENCES

6.1 REVIEWS

1. *OSE Review # 2006-821, Proprietary Name, Label and Labeling Review for Intuniv (Guanfacine Hydrochloride) Tablets, Fava, W; April 18, 2007.*

6.2 DATABASES

1. *Micromedex Integrated Index (<http://csi.micromedex.com>)*

Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. *Phonetic and Orthographic Computer Analysis (POCA)*

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. *Drug Facts and Comparisons, online version, St. Louis, MO (<http://factsandcomparisons.com>)*

Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. *AMF Decision Support System [DSS]*

DSS is a government database used to track individual submissions and assignments in review divisions.

5. *Division of Medication Errors Prevention and Analysis proprietary name consultation requests*

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

6. *Drugs@FDA (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)*

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved [brand name](#), [generic drugs](#), [therapeutic biological products](#), [prescription](#) and [over-the-counter](#) human drugs and [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

7. *Electronic online version of the FDA Orange Book (<http://www.fda.gov/cder/ob/default.htm>)*

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. *U.S. Patent and Trademark Office (<http://www.uspto.gov>)*

USPTO provides information regarding patent and trademarks.

9. *Clinical Pharmacology Online* (www.clinicalpharmacology-ip.com)

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

10. *Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at* (www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. *Natural Medicines Comprehensive Databases* (www.naturaldatabase.com)

Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. *Stat!Ref* (www.statref.com)

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

13. *USAN Stems* (<http://www.ama-assn.org/ama/pub/category/4782.html>)

USAN Stems List contains all the recognized USAN stems.

14. *Red Book Pharmacy's Fundamental Reference*

Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. *Lexi-Comp* (www.lexi.com)

Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

16. *Medical Abbreviations Book*

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The medication error staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The medication error staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The medication error staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc), along with other

orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the medication error staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	Considerations when searching the databases		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B: Proprietary names lacking convincing orthographic similarity with Intuniv

Proprietary name	Similarity to Intuniv
Enjuvia	Look
Entereg	Look
Invanz	Look
Imodium	Look

Appendix C: Foreign Proprietary Names with Similarity to Intuniv

Proprietary Name	Similarity to Intuniv	Country where Marketed
Introcin	Look	Canada
Interac	Look	Phillipines
Entumin	Look and Sound	Italy
Intrinsa	Look	United Kingdom, Ireland, Germany, France and Spain

Appendix D: Foreign Proprietary Name for Intuniv

Proprietary Name	Country where trademarked	Trademark Owner
Entuniv	Canada	Shire Pharmaceuticals

Appendix E: Discontinued proprietary names with orthographic similarity to Intuniv with no generic alternative available

Proprietary name (established name) strength	Similarity to Intuniv	Status
Actinex (masoprocol) 10%	Look	Discontinued June 1996

Appendix F: Products with orthographic/phonetic similarity to Intuniv but no overlap in strength and dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength/Dosage Form	Usual Dose (if applicable)																			
Intuniv (guanfacine hydrochloride)	N/A	1 mg, 2 mg, 3 mg, 4 mg extended-release tablets	1 mg to 4 mg once daily																			
Indinavir (established name for Crixivan)	Look	100 mg, 200 mg, 333 mg, and 400 mg capsules	800 mg three times daily																			
Indocin (indomethacin) Indocin I.V. (indomethacin sodium trihydrate)	Look	25 mg/5 mL oral suspension; 25 mg and 50 mg capsules; 75 mg Extended-release capsules; 50 mg rectal suppositories 1 mg powder for injection single dose vial	<u>Moderate to severe rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, and acute bursitis or tendonitis:</u> 25 mg 2 or 3 times a day. If tolerated, gradually increase the dose until satisfactory response is obtained or until a total daily dose of 150 mg to 200 mg is reached. <u>Acute gouty arthritis:</u> 50 mg 3 times per day until pain is tolerable. Then rapidly taper off the drug. <u>Patent ductus arteriosus:</u> (Intravenous only): Three I.V. doses given at 12 to 24 hour intervals. Dosage according to age at first dose is as follows: <table border="1"> <thead> <tr> <th rowspan="2">Age at 1st dose</th> <th colspan="3">Dosage (mg/kg)</th> </tr> <tr> <th>1st</th> <th>2nd</th> <th>3rd</th> </tr> </thead> <tbody> <tr> <td>Less than 48 hrs</td> <td>0.2</td> <td>0.1</td> <td>0.1</td> </tr> <tr> <td>2 to 4 days</td> <td>0.2</td> <td>0.2</td> <td>0.2</td> </tr> <tr> <td>Over 7 days</td> <td>0.2</td> <td>0.25</td> <td>0.25</td> </tr> </tbody> </table>	Age at 1 st dose	Dosage (mg/kg)			1 st	2 nd	3 rd	Less than 48 hrs	0.2	0.1	0.1	2 to 4 days	0.2	0.2	0.2	Over 7 days	0.2	0.25	0.25
Age at 1 st dose	Dosage (mg/kg)																					
	1 st	2 nd	3 rd																			
Less than 48 hrs	0.2	0.1	0.1																			
2 to 4 days	0.2	0.2	0.2																			
Over 7 days	0.2	0.25	0.25																			
Imatinib (established name for Gleevac)	Look	100 mg and 400 mg tablets	<u>Adults with CML:</u> 400 mg to 600 mg once daily <u>Children with CML:</u> 260 mg/m ² once daily or the daily dose may be divided into 2 doses																			
Intron A (interferon alfa-2b)	Look	10 million IU, 18 million IU, 50 million IU Powder for Injection Solution for Injection: 6 million IU/1 mL, 10 million IU/1 mL, 25 million IU/2.5 mL <u>Single-dose Pens:</u>	<u>Hairy-cell leukemia:</u> 2 million IU/m ² IM or SC 3 times/week for up to 6 months. <u>AIDS-related Kaposi's sarcoma:</u> 30 million IU/m ² 3 times/week administered SC or IM. <u>Hepatitis B:</u> 30 to 35 million IU/week SC or IM, either as 5 million IU daily or																			

		3 million IU/0.2 mL, 5 million IU/0.2 mL, 10 million IU/0.2 mL <u>Multidose Pens</u> : 3 million, 5 million, and 10 million international units per dose	10 million IU 3 times/week for 16 weeks. <u>Hepatitis C</u> : 3 million IU 3 times/week SC or IM for 16 weeks; extend therapy 18 – 24 months if tolerated. <u>Malignant Melanoma</u> : 20 million IU/m ² IV infusion on 5 consecutive days/week for 4 weeks. Maintenance dosage is 10 million IU/m ² SC
Emtriva (emtricitabine)	Look	200 mg capsules	200 mg once a day
Antara (fenofibrate)	Look	43 mg or 130 mg capsules	43 mg or 130 mg by mouth once daily
Intal (cromolyn sodium)	Look	20 mg/2 mL nebulizer solution	20 mg inhaled by mouth four times a day
Intelence (etravirine)	Look	100 mg capsule	200 mg by mouth twice a day after a meal

(b) (4)

Interex (multiple ingredient homeopathic product)	Look	187.5 mg Epimedium grandiflorum extract, 75 mg muira puama extract, 75 mg maca, 75 mg L-Arginine HCl USP, 37.5 mg Tribulus terrestris extract, 37.5 mg mucauna pruriens extract, 37.5 mg coleus forskolin	No additional information found
Intropin (dopamine hydrochloride)	Look	40 mg/mL, 80 mg/mL, and 160 mg/mL injectable	400 mg in 250 mL D5W infused intravenously at a rate of 20 mcg/kg/min
Lotrisone (clotrimazole/betamethasone)	Look	1%/0.05% topical cream, lotion	Apply to affected area twice a day
Lotrimin (clotrimazole)	Look	1% topical cream, topical solution 10 mg troche	Apply to affected area twice a day Dissolve one troche in mouth five times a day for 14 days.
Infanrix (diphtheria/tetanus/pertussis)	Look	Suspension for injection	Inject 0.5 mL intramuscularly at 8 weeks of age, then at 4 to 8 week intervals for a total of 3 doses. Adults: Inject 0.5 mL intramuscularly x1 dose

<p>Infuvite (multivitamin complex)</p>	<p>Look</p>	<p>Adult: 3,300 IU Vitamin A, 200 IU Vitamin D, 10 IU Vitamin E, 6 mg Vitamin B1, 3.6 mg Vitamin B2, 40 mg Vitamin B3, 15 mg Vitamin B5, 6 mg Vitamin B6, 5 mcg Vitamin B12, 200 mg Vitamin C, 60 mcg biotin, 600 mg folic acid</p> <p>Pediatric: 2,300 IU Vitamin A, 400 IU Vitamin D3, 7 IU Vitamin E, 1.2 mg Vitamin B1, 1.4 mg vitamin B2, 17 mg Vitamin B3, 5 mg Vitamin B5, 5 mg Vitamin B6, 1 mcg Vitamin B12, 80 mg Vitamin C, 20 mcg biotin, 140 mg folic acid</p>	<p>Adult: 10 mL diluted in intravenous fluid daily as indicated by laboratory results</p> <p>Pediatric: 5 mL diluted in intravenous fluid daily as indicated by laboratory results</p>
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Appendix G: FMEA Table.

Intuniv (guanfacine hydrochloride)	1 mg, 2 mg, 3 mg, 4 mg extended-release tablets	Usual Dose: 1 mg to 4 mg by mouth daily
Failure Mode: Name confusion	Causes (could be multiple)	Effects
<p>Entecavir (established name for Baraclude)</p> <p>0.05 mg/mL solution</p> <p>0.5 mg tablet</p> <p>1 mg tablet</p>	<p>Orthographic similarities include:</p> <p>Beginning three letters of both names look similar when scripted:</p> <p>‘ent’ vs. ‘int’</p> <p>Overlapping strengths:</p> <p style="text-align: center;">1 mg</p> <p>Overlapping dosage forms:</p> <p style="text-align: center;">oral tablets</p> <p>Overlapping frequency of administration:</p> <p style="text-align: center;">Once a day</p>	<p>Orthographic differences and different product characteristics between these two products will minimize the potential for confusion that may lead to medication errors.</p> <p><i>Rationale:</i></p> <p>Entecavir contains 9 letters compared to 7 letters in Intuniv and appears longer when scripted.</p> <p>Ending letter string ‘avir’ in Entecavir looks dissimilar to the ending letter string ‘univ’ in Intuniv.</p> <p>The setting of use may help minimize confusion between these two products since Entecavir is indicated for the treatment of chronic hepatitis B, whereas Intuniv is indicated for the treatment of Attention Deficit Hyperactivity Disorder which is predominantly in a pediatric population where hepatitis B would be less prevalent.</p>
<p>Insulin</p> <p>injectable available in many different formulations (solution vs suspension) and under many different proprietary names</p>	<p>Orthographic similarities include:</p> <p>Both names begin with the same two letters, ‘in’</p> <p>Both names contain seven letters and appear similar in length when scripted.</p> <p>Both names have two upstroke letters:</p> <p style="text-align: center;">‘I’ and ‘t’ in Intuniv</p> <p style="text-align: center;">vs</p> <p style="text-align: center;">‘I’ and ‘l’ in Insulin</p>	<p>Orthographic difference and differing product characteristics will minimize the potential for confusion between these two products that may lead to medication errors.</p> <p><i>Rationale:</i></p> <p>Intuniv contains the crosstroke letter, ‘t’ which Insulin does not have.</p> <p>The location of the second upstroke letters in both names are in different positions</p> <p style="text-align: center;">I n t u n i v</p> <p style="text-align: center;">I n s u l i n</p> <p>Insulin is a parenteral product vs Intuniv which is an oral extended-release tablet, so the different routes of administration would minimize potential confusion between the two products.</p> <p>The proprietary name ‘Insulin’ is available in many</p>

		<p>different formulations and it is necessary for prescribers to include specific prefixes (such as NPH or Regular) and suffixes (such as glargine), on insulin orders.</p> <p>The units of measure for Insulin are in ‘units’ versus the units of measure for Intuniv which are in milligrams.</p> <p>The products also have different dosage forms, parenteral vs oral and different routes of administration, which may also help to differentiate them on written orders.</p>
<p>Guanfacine hydrochloride (established name for Tenex) immediate-release tablets</p>	<p>Overlapping established names: Guanfacine hydrochloride</p> <p>Overlapping strengths: Tablets: 1 mg and 2 mg</p> <p>Overlapping doses: 1 mg or 2 mg once a day</p>	<p>Intuniv has the proposed indication of attention deficit hyperactivity disorder in children between 6 years of age to 17 years of age, whereas currently marketed guanfacine is approved for treatment of hypertension in adults. The relative bioavailability of Intuniv to immediate release guanfacine is 58%, both dosage formulations are dosed once a day, and there are numerous generic equivalents available, thus, it is less likely for prescribers to switch patients taking immediate release guanfacine for hypertension to Intuniv because there are no benefits.</p>

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Walter Fava
5/5/2009 03:27:16 PM
DRUG SAFETY OFFICE REVIEWER

Carlos M Mena-Grillasca
5/5/2009 03:28:44 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
5/5/2009 04:58:17 PM
DRUG SAFETY OFFICE REVIEWER